REMARKS

Introduction

Claims 1-20 are pending. Claims 1, 4, 8, 12 and 13-14 have been amended. Support for these amendments can be found throughout the specification, for example, in the original claims and at Example 1. No new matter has been added.

Objection to claim 4

The Examiner has requested correction of the term "Triton" as it appears in claim 4. This term has been replaced with "Triton X-100" in amended claim 4. This objection is moot and its withdrawal is respectfully requested.

New Matter Rejection under 35 U.S.C. §112

The Examiner has rejected claim 12 under the first paragraph of 35 U.S.C. §112 as allegedly containing new matter. Specifically, the Examiner asserts that the phrase "wherein the active form of A1AT has a maximum activity of 100%" is new matter. Applicants traverse.

To expedite prosecution, claim 12 has been amended to recite that "the plasma-like form of A1AT has a maximum activity of 100%." One of skill in the art knows that the A1AT activity of natural plasma is 100%. For example, Mattes *et al.* disclose that an active-inactive ratio of A1AT of at least 120% is greater than the ratio found in plasma. See the Abstract. Further, Mattes *et al.* state that the "relative plasma alpha1-AT activity is defined as the ratio of active to inactive alpha1-AT, this ratio in plasma being assumed to be 100% of relative plasma alpha1-AT activity." See page 6 of AU 199874180 (a corresponding English language publication to the WO Mattes *et al.* document cited by the Examiner in the Office Action). Thus, one of skill in the art, as shown in Mattes *et al.*, would know that natural plasma has an A1AT activity of 100%.

The A1AT isolated using the techniques disclosed and claimed in the current application has the same molecular weight as natural A1AT (see Figure 1 of the specification) as well as the

same "plasma-like" activity. The SDS-PAGE presented in the specification reveals the high purity of the A1AT preparation after the removal of the detergent (see lane 3 of the scanned PAGE in Figure 1 of the specification).

As described in the assay and experimental data below, the nativity of an isolated preparation of the claimed invention was assessed by quantifying the A1AT antigen and the A1AT activity. The results are shown in Table 1 below.

A1AT activity assay

A1AT activity is determined by means of the physiologically relevant reactions of elastase inhibition. A complex of AlAT and elastase (ratio 1:1) is formed when excess amounts of elastase is added to the sample. The residual activity of elastase is able to cleave pNA from the substrate N-succinyl-$(Ala)_3$-pNA and this reaction is measured kinetically at 405 nm for 100 seconds at 37°C. The activity is measured against a standard (prepared from the commercially available PROLASTIN®) and the concentration of A1AT is inversely proportional to the rate of the elastase activity.

A1AT antigen assay

Capture antibodies to human A1ATI (e.g. rabbit anti human A1AT) are bound to the surface of microtiter plates. Samples at various dilutions were incubated and A1-AT captured by the antibodies; then this complex is marked by a second antibody preparation conjugated with peroxidase (e.g. Sheep-Anti-Human A1AT x PO). The enzyme of the conjugate turns the color of the staining solution to yellow. The reaction is stopped by the addition of sulphuric acid and the orange color is measured at 492nm. The unknown A1AT content in the samples in then calculated from intensities of a calibrator with known amount of A1AT (e.g. N7/T Protein Control SL/L conc. Low; Dade Behring) tested in parallel.

Results

Three independent MAT preparations were analyzed revealing activity/antigen ratios close to 1 (see col.4 of table 1), which proved that essentially all A1AT was prepared in its active state, corresponding to "plasma-like" activity.

Table 1

Preparation	AlAT:Activity (mg/ml)	A1AT:Antigen (mg/ml)	Ratio Activity/Antigen (mg/mg)
1	34.8	35.1	0.99
2	33.0	33.6	0.98
3	32.0	33.8	0.95

In view of the above data, Applicants believe that rejection under 35 U.S.C. §112 for allegedly claiming new matter has been overcome. Applicants respectfully request that this rejection be withdrawn.

Enablement Rejection under 35 U.S.C. §112

The Examiner has rejected claims 1-5, 9-11, and 13-17 under 35 U.S.C. §112 as allegedly failing to provide enablement for the claimed ranges in the process. Applicants traverse.

The specification provides a working example of the claimed process in Example 1. The specification further describes the methods, including reagents used, and the desired results of some embodiments of the claimed process in paragraphs [0019], [0021], and [0026]-[0033]. When the specification as a whole is considered, including the working example, Applicants respectfully assert that one of skill in the art would be able to make or use the claimed invention without undue experimentation.

Indefinite Rejection under 35 U.S.C. §112

The Examiner has rejected claims 1-20 under 35 U.S.C. §112 as allegedly being indefinite because of the language recited in the preamble. The Examiner has also requested clarification of the language in claims 8 and 13-14. Applicants traverse.

To expedite prosecution, the preamble of independent claim 1 has been amended to clarify that the A1AT is purified from other protein components in an A1AT containing solution. Claims 8 and 13-14 have also been amended to address the Examiner's concerns. Applicants believe this rejection is now moot. Withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. §102

The Examiner has rejected claims 12-18 and 20 under 35 U.S.C. §102(b) as allegedly being anticipated by Mattes *et al.* (AU 199874180 B2; WO9856821). Applicants traverse.

To expedite prosecution, claim 12 has been amended to recite that "the plasma-like form of A1AT has a maximum activity of 100%." In contrast, Mattes *et al.* discloses a method of preparation of A1AT having an activity of at least 120%., which is greater than that in plasma. This increased activity results from a greater ratio of active to inactive A1AT in the preparation than is present in plasma. See the Abstract of Mattes.

The Examiner has also rejected claims 1-5 and 9-11 as allegedly being anticipated by Taniguchi *et al.* Applicants traverse.

To expedite prosecution, claim 1 has been amended to clarify the order of the steps in the claimed method. The claimed method of purifying involves salting the detergents out after treatment (e.g., applying the salt to the elution of the ion-exchange chromatography), as disclosed in Example 1. In contrast, Taniguchi *et al.* discloses the addition of a detergent (polysorbital 80) which is followed by cooling the solution, adjusting the pH, applying the solution to a copper chelating medium and then washing the resulting medium with NaCl solution. This reference does

not disclose a salting out step directly after the addition of a detergent as amended claim 1 requires. Thus, Taniguchi *et al.* does not anticipate claims 1-5 and 9-11 because it does not disclosed the claimed method in the order the steps have been claimed.

For at least the above reasons, the cited documents do not anticipate the claims. Therefore, the rejection of claims 1-5, 9-11, and 12-19 under 35 U.S.C. §102 is improper and its withdrawal is respectfully requested.

Rejection under 35 U.S.C. §103

Claims 6-8 have been rejected under 35 U.S.C. §103(a) as allegedly being obvious in view of Taniguchi *et al.* and Isaksson *et al.* Applicants traverse.

As discussed above, Taniguichi *et al.* does not discuss the step of "salting out" the detergents in the claimed order. This deficiency is not remedied by Isaksson *et al.* which deals with a process for the reduction of virus inactivation chemicals. See Abstract. Isaksson *et al.* discloses the removal of detergents using a sodium citrate method, but its final product is medically unacceptable because, as seen in Example 4, it comprises 250 ppm Triton X-100 and 35 ppm TNBP. Thus, one of skill in the art would be taught away from using the methods of Isaksson *et al.* in an A1AT purification scheme because of the high levels of residual detergents which render the purified product unacceptable for medical applications.

Therefore, as the Examiner notes in the Office Action, because Taniguichi *et al.* does not teach a pasteurization step or a step involving immobilized heparin (e.g., in a gel) it would not have been obvious for one of skill in the art to arrive at the claimed invention, even in view of Isaksson *et al.* Further, the combination of Taniguichi *et al.* and Isaksson *et al.* simply does not teach or suggest the claimed process in the order the steps are claimed. For at least the above reasons, the rejection of claims 6-8 under 103(a) is improper and its withdrawal is respectfully requested.

The Examiner has also rejected claim 19 as allegedly being obvious under 35 U.S.C. §103(a) in view of Mattes *et al.* As discussed previously, Mattes *et al.* does not disclose or teach

the claimed A1AT having the "plasma-like" activity set forth in claim 12, from which claim 19 depends. Therefore, by virtue of its dependency on claim 12, claim 19 is not obvious in view of Mattes *et al.* and withdrawal of this rejection is respectfully requested.

CONCLUSION

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. Accordingly, Applicants request that the Examiner issue a Notice of Allowance indicating the allowability of the claims and that the application be passed to issue. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is hereby invited to telephone the undersigned at the number provided.

The Commissioner is authorized to charge any deficiency in any patent application processing fees pursuant to 37 CFR §1.17, including extension of time fees pursuant to 37 CFR §1.17(a)-(d), associated with this communication and to credit any excess payment to Deposit Account No. 22-0261.

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Respectfully submitted,

By _____

Matthew E. Kelley
Registration No.: 55,887
VENABLE LLP
P.O. Box 34385
Washington, DC 20043-9998
(202) 344-4000
(202) 344-8300 (Fax)
Attorney/Agent For Applicant

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